

The erythromycin PKS

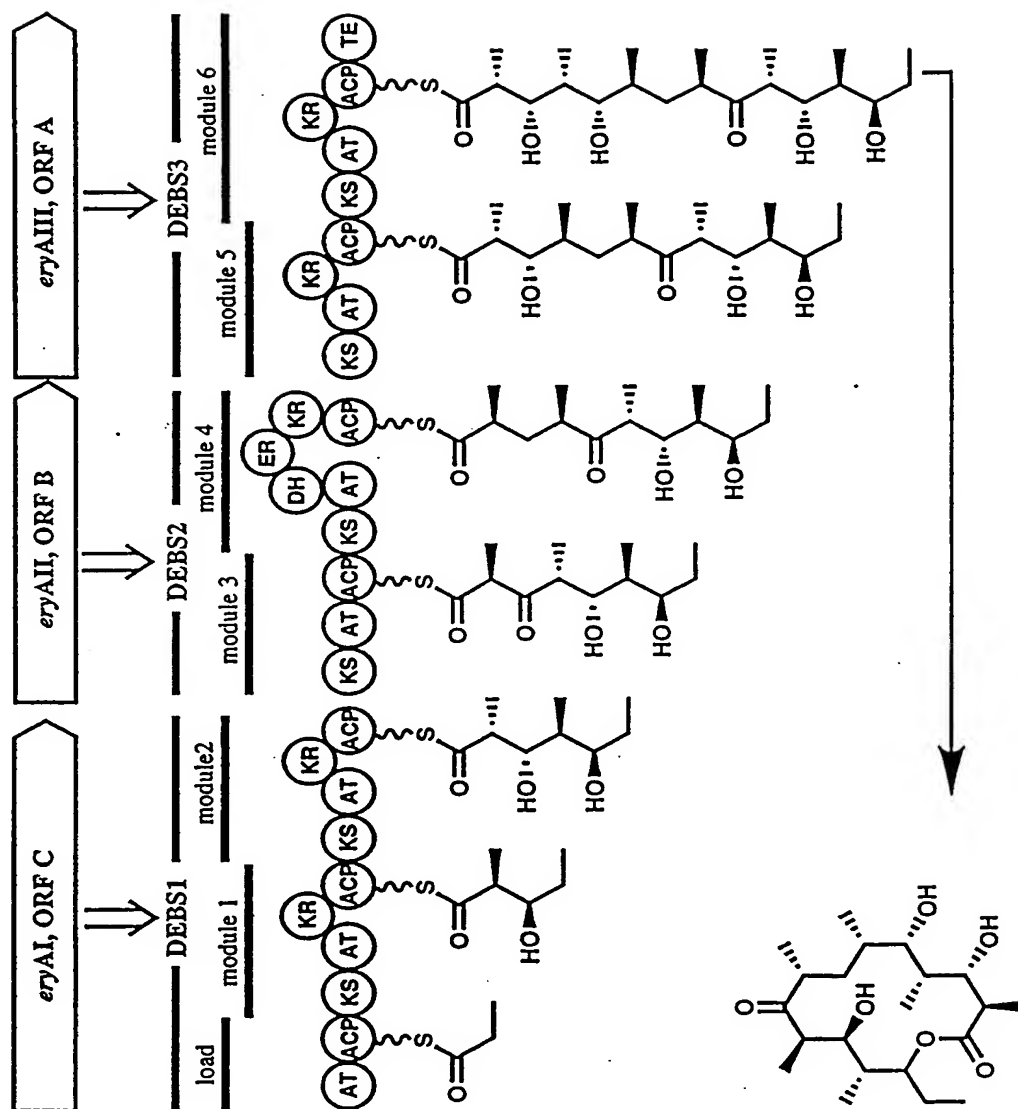


Fig. 1

2/12

KCLFDAU
KCLFPEU
KCLFACT
KCLFHIR
KCLFGRA
KCLFNOG
KCLFTCM
KCLFCIN
KCLFVNZ
KCLFWHIE
KSGRA
KSHIR
KSACT
KSCIN
KSVNZ
KSNOG
KSTCM
KSDAU
KSPEU
KSWHI

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-----MSVLTITGVGVVAPNGLGLAPYWSAVLDGRHGLGPVT
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-----MTAAVVVTGLGVVAPTGLGVREHWSSTVRGASAI GPVT
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-----MTP-VAVTGMGLAAPNGLGRPTTGRPPWAPRAASAAS
-----MSASVVVTGLGVVAPNGLGREDFWASTLGGKSGIGPLT
-----MSGPQRTGTGGSSRRRAVVTGLGVLSPHGTGVEAHWKAVADGTSSSLGPVT
-----MTRRVVITGVGVVAPGGSGTKEFWDLLTAGRTATRPIS
-----MTRRVVITGVGVVAPGGGLGAKNFWELLTSGRTATRRIS
-----MKRRVVITGVGVVAPGGNGTRQFWELLTSGRTATRRIS
-----MTQRRVAITGIEVLAPGGGLGRKEFWLLSEGRATRGIT
-----MTARRVVITGIEVLAPGGTGSKAFWNLLSEGRATRGIT
-----MKESINRRVVITGIGIVAPDATGVKPFWDLLTAGRTATRTIT
-----MTRHAEKRVVITGIGIVVAPGGAGTAAFWDLLTAGRTATRTIS
-----MNRRVVITGMGVVAPGAIGIKSEFWELLTSGTTATRAIT
-----MNRIVITGIGIVVAPGAVGTPKFWEELLTSGTTATRAIS
-----MTRRRVAVTIGIVVAPGGIGTPQFWRLLSEGRATRRIS

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KCLFPEU
KCLFACT
KCLFHIR
KCLFGRA
KCLFNOG
KCLFTCM
KCLFCIN
KCLFVNZ
KCLFWHIE
KSGRA
KSHIR
KSACT
KSCIN
KSVNZ
KSNOG
KSTCM
KSDAU
KSPEU
KSWHI

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RFTGDGRLGRLAGEVSDFVP-EDHLPKRLLAQTDPMQY-ALAAAEWALREAGCAPSS--
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RFDPTGYPAELAGQVLDFA-TEHLPKRLLPQTDVSTRF-ALAAADWALADAGVGPESGL
RFDASRYPSRLAGQIDDFEA-SEHLPKRLLPQTDVSTRY-ALAAADWALADAGVGPESGL
RFDAGRYPSKLAGEVPGFVP-EDHLPKRLLPQTDHMTL-ALVAADWAFQDAAVDP SK-L
RFDPHGYPVRVGGEVLAFDA-AAHLPGRLLPQTDRTQH-ALVAAEWALADAGLEPEK-Q
RFDPSGYPAQLAGEIPGFRA-AEHLPGRLVPQTDRTVRL-SLAAADWALADAGVEVAA-F
RFDPTGYPARLAGEVPGFAA-EEHLPKRLLPQTDRTMRL-ALVAADWALADAGVRPEE-Q
REGCAHLPLRVAGEVHGFA-AETVEDRFLVQTDRTFTHF-ALSATQHALADARFGRADVD
FFDASPFRSRIAGEI-DFDAVAEGFSPREVRMDRATQF-AVACTRDALADSGLD TGA-L
FFDPTPNRSQIAAEC-DFDPEHEGLSPREIRMDRAAQF-AVCTRDALADSGLEFEQ-V
FFDPSPYRSQVAAEA-DFDPVAGFGPRELDRMDRASQF-AVACAREAFASGLDPDT-L
FFDPAPFRSKVAAEA-DFCGLNGLSPQEVRRMDRAAQF-AVVTAR-AVEDSGAELAA-H
FFDPTPFRSRVAAEI-DFDPEAHGLSPQEIIRMDRAAQF-AVVAAR-AVADSGIDLAA-H
AFDPSPFERSRIAAEC-DFDPLAEGLTPOQIRMDRATQF-AVVSARESLD SGLDLGA-L
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TFDATPFRSRIAAEC-DFDPVAGLSAEQARRLDRAQF-ALVAGQEALD SGLRIGE-D
TFDATPFRSRIAAEC-DFDPVAGLSAEQARRLDRAQF-ALVAGQEALD SGLRIGE-D
LFDPSGLRSQIAAEC-DFEPSDHGLGLATAQRCDRYVQF-ALVAASEAVRDANLDMNR-E

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Fig 2A

KCLFDAU
KCLFPEU
KCLFACT
KCLFHIR
KCLFGR A
KCLFNOG
KCLFTCM
KCLFCIN
KCLFVNZ
KCLFWHIE
KSGRA
KSHIR
KSACT
KSCIN
KSVNZ
KSN OG
KSTCM
KSDAU
KSPEU
KSWHI

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- PLEAGVITASASGGFASGQRELQNLWSKG-----PAHVSAYMSFAWFY-AVNTGQIAIR
- PLEAGVITASASGGFAFGQRELQNLWSKG-----PAHVSAYMSFAWFY-AVNTGQIAIR
TDYDMGVVTANACGGFDFTHREFRKLWSEG-----PKSVSVYESFAWFY-AVNTGQISIR
PEYGTGVI TSNATGGFEFTHREFRKLWAQG-----PEFVSVYESFAWFY-AVNTGQISIR
DDYDGVVSTTAQGGFDFTHREFHKLWSQG-----PAYVSVYESFAWFY-AVNTGQISIR
PEYLGVVVTAASSAGGFEGFHRELQNLWSLG-----PQVVSAYQSFAPWFY-AVNTGQVSIR
DEYGLGVLTAAGAGGFEFGQREMOKLWGTG-----PERVSAYQSFAPWFY-AVNTGQISIR
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SPYSVGVVTAAGSGGGEGFGQRELQNLWGHG-----SRHVGPYQSIAPWFY-AASTGQVSIR
DPSRIGVALGSASAVATSLENEYLVMSDSGREWLVDPAHLSPMFDFYLSPGVMPAEVAWA
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DPYRVGVTVGSAVGATMGLDEEYRVVSDGGRLDLVDHAYAVPHLYDYFVPPSSFAEVAWA
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SAHRVGVCVGTAVGCTQKLESEYVALSAGGAHVVDPGRGSELYDYFVPPSSLAAEVAWL
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KCLFDAU
KCLFPEU
KCLFACT
KCLFHIR
KCLFGRA
KCLFNOG
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KCLFVNZ
KCLFWHIE
KSGRA
KSHIR
KSACT
KSCIN
KSVNZ
KSNOG
KSTCM
KSDAU
KSPEU
KSWHI

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-HDLRGPVGVVVAEQAGGLDALAHAR-RKVRGGAE-LIVSGAVDSSLCP-YGMAAQVKS
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-HGLRGP GSVLVAEQAGGLDAVGHG--AVRNGTP-MVVTGGVDSSFPD-WGWVSHVSS
-NIMRGP SAALVGEQAGGLDAIGHAR-RQLRRPG-WCSAVASTRRSTR-GASSSQLSG
-HGLRGP GSVLVT EQAGGLDALGQAR-RQLRRGLP-MVVGAVDGSFPCP-WGWVQQLSS
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-AGAEGPVTM/SDGCTSGLDSVGYAV-QGTREGSADVVAGAADTPVSPITVACFDAIKA
-VGAEGPVM/MSDGTSGLDSL SHAC-SLIAEGTTDVMVAGAADTPITPITVACFDAIKA
-VGAEGPVTM/STGCTSGLDSVGNV-RAIEEGSADVMFAGAADTPITPITVACFDAIRA
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-VGAEGPNTVSTGCTSGLDSVGYARGELIREGSADVMLAGSSDAPISPIITMACFDAIKA
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KCLFDAU
KCLFPEU
KCLFACT
KCLFHIR
KCLFGRA
KCLFNOG
KCLFTCM
KCLFCIN
KCLFVNZ
KCLFWHIE

RLSGSDPTAGYLPFDRRAAGHVPGE-GAILAVEDAERVAERG-GKVGSIAGT-ASF
RLSGSDNPTAGYLPFDRRAAGHVPGE-GAILTVEDAERAAERG-AKVGSIAGYGASFD
RISTATDPDRAYLPFDERAAGYVPGE-GAILVLEDSAAAEARGRHDAYGELAGCASTFD
RVSRATDPGRAYLPFDVAANGYVPGE-GAILLLEDAESAKARG-ATGYGEIAGYAATFD
LVSTVADPERAYLPFDVDASGYVPGE-GAVLIVEDADSARARG--AERIYVRSPLRFD
GLSTSDDPRRAYLPFDAAAGGHVPGE-GALLVLESDESARARGVTRWYGRIDGYAATFD
FLSEATDPHDAYLPFDRAAGHYVPGE-GAMLVAERADSARERDAATVYGRIGHASTFD
-MSDSDPNRAYLPFDRDGRGYVPGGGRGVVPLERAEAAPARG-AEYVGE-AGPLARL-
RLSTSEEPARGYLPFDREAQGHVPGE-GAILVMEAAEAARERG-ARIYGEIAGYGSTFD
ELSRATEPDRAYRPFTEACGFAPAEG-GAVLVVEEEAAARERG-ADVTRATVAGHAATFT

Fig 2B

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KSGRA	TTPRNDDPAHASRPFDDGTRNGFVLAEG-AAMFVLEEEYEAQRRG-AHIYAEVGGYATRSQ
KSHIR	TTPRNDDPEHASRPFDDNSRNGFVLAEG-AALFVLEEELEHARARG-AHVYAEISGCATRLN
KSACT	TTARNDDPEHASRPFDDGTRDGFVLAEG-AAMFVLEEDYDSALARG-ARIHAEISGYATRCN
KSCIN	TTPRHDAPATASRPFDDSTRNGFVLGEG-AAFFVLEELHSARRRG-AHIYAEIAGYATRSN
KSVNZ	TTNRYDDPAHASRPFDDGTRNGFVLGEG-AAVFLVLEELHESARARG-AHIYAEIAGYATRSN
KSNOG	TTPRNDDPAEASRPFDDTRNGFVLGEG-AAVFLVLEEFHARRRG-ALVYAEIAGFATRCN
KSTCM	TSANNDPAHASRPFDDNRDGFVLGEG-SAVFVLEELSAARRRG-AHAYAEVRGFATRSN
KSDAU	TSDHNDTPETLA-PFSRSRNGFVLGEG-GAIVVLEEEAAVRRG-ARIYAEIGGYASRGN
KSPEU	TSDHNDTPETASRPFDDSRNGFVLGEG-GAIVVLEEEAAVRRG-ARIYAEIGGYASRGN
KSWHI	TSPNNDPAHASRPFDDADRNCFVMGEG-AAVLVLEEDLEHARARG-ADVCEVSGYATFGN
	* ** * . . . * . . . *
KCLFDAU	-PPPGSGRP---SALARAVETALADAGLDRSDIAVVFADGAA-VGELDVAAEAEALASVFG
KCLFPEU	-PPPGSGRP---SALARAVETALADAGLDGSDIAVVFADGAA-VPELDAAEAEALASVFG
KCLFACT	-PAPGSGRP---AGLERAIRLALNDAGTGPEVDVVFADGAG-VPELDAAEAEARIGRVFG
KCLFHIR	-PAPGSGRP---PALRRRAIELALADAELRPEQVDVVFADAG-VAELDAIEAAAIRELFG
KCLFGRA	-PAPGSGRP---PALGRAAEALALAEAGLTPADISVVFADGAG-VPELDRAEADTLARLFG
KCLFNOG	-PPPGSGRP---PNLLRAAQALDDAEVGPFAVDVVFADAG-TPEDAAEADAVRRLFG
KCLFTCM	-ARPGTGRP---TGPARAIRLALAEARVAPEDVDVVFADAG-VPALDRAEAEALAEVFG
KCLFCIN	-PAPHSGRG---STRAHAIRLALDAGTAPGDIRRVFADGGGYPN-DRAEAEAISEVFG
KCLFVNZ	-PRPGSGRE---PGLRKAIELALADAGAAPGDIDVVFADAAA-VPELDRAEAEALNAVFG
KCLFWHE	GAGRWAESR---EGLARAIQALAEAGCRPEEVDVVFADALG-VPELDRAEAEALADALG
KSGRA	-AYHMTGLKKGREMAEAI RVALDLARIDPTDIDYINAHGSG-TKQNDRHETAFAFKRSLG
KSHIR	-AYHMTGLKTDGREMAEAI RVALDLARIDPTDIDYINAHGSG-TKQNDRHETAFAFKRSLG
KSACT	-AYHMTGLKADGREMAEAI RVALDESRTDIDYINAHGSG-TRQNDRHETAFAFKRSLG
KSCIN	-AYHMTGLR-DGAEMAEAI RVALDEARNPTEIDYINAHGSG-TKQNDRHETAFAFKRSLG
KSVNZ	-AYHMTGLRDPGAEMAEAI RVALDEARNPTEIDYINAHGSG-TKQNDRHETAFAFKRSLG
KSNOG	-AFHMTGLRDPGAEMAEAI GVALAQAGKAPADVDYVNAHGSG-TRQNDRHETAFAFKRSLG
KSTCM	-AFHMTGLKPDGREMAEAI TAALDQARRTGDDLHYINAHGSG-TRQNDRHETAFAFKRSLG
KSDAU	-AYHMTGLRADGAEMAAAI TAALDEARRDPSVDYVNAHGTA-TRQNDRHETAFAFKRSLG
KSPEU	-AYHMTGLRADGAEMAAAI TAALDEARRDPSVDYVNAHGTA-TQQNDRHETAFAFKRSLG
KSWHI	-AYHMTGLTKEGLEMAEAI TALDMAELDGSADYVNAHGSG-TQQNDRHETAFAFKRSLG
	. : : : ** : : : * . . . * * : : *

Fig 2c

5/12

KCLFDAU
KCLFPEU
KCLFACT
KCLFHIR
KCLFGRA
KCLFNOG
KCLFTCM
KCLFCIN
KCLFVNZ
KCLFWHIE
KSGRA
KSHIR
KSACT
KSCIN
KSVNZ
KSNOG
KSTCM
KSDAU
KSPEU
KSWHI

P--HRVPVTVPKLTGRLYSGAGPLDVATGLLALRDEVVPATGHVH-PDPDLPLDVVTGR
P--RRVPVTVPKLTGRLYSGAGPLDVATALLALRDEVVPATAHVD-PDPDLPLDVVTGR
R--EGVPVTVPKTTTGRLYSGGGPLDVVTALMSLREGVIAPTAGVTSVPREYGIDLVLGE
P--SGVPVTAPKMTGRLYSGGGPLDLVAALLAIRDQVIPPTVHTAEPVPEHQDLVTGD
P--RGVPVTAPKALTGRLCAGGGPADLAAALLALRDQVIPATGRHRAVPDAYALDLVTGR
P--YGVVTVAPKMTGRLSAGGAALDVATALLALREGVVPPTVNVSRPRPEYELDLVLA-
P--GAVPVTAPKMTGRLYAGGAALDVATALLSIRDCVVPPTVGTGAPAPGLGIDLVLHQ
P--GRVPVTCPRMTGRLHSGAAPLDVACALLAMRAGVIPPTVHID-PCPEYDLDLVLYQ
T--GAVPVTAPKMTGRLYSGAAPLDLAAFLAMDEGVIPTVNVE-PDAAYGLDLVVGG
PHAARVPVTAPKTGTGRAYCAAPVLDVATAVLAMEHGLIPTPHVL--DVCHDLDLVTGR
EHAYAVPVSSI KSMGHS LGAGSIEIAASVLAIEHNVVPPTANLHTPDPECDLDYVPLT
EHAYRTPVSSI KSMVGHSLGAGSIEVAACALAI EHGVPPTANLHEPDPECDLDYVPLT
EHARRTPVSSI KSMVGHSLGAGSLEIAACVLALEHGVPPTANLRTSDPECDLDYVPLE
EHAYRTPVSSI KSMVGHSLGAGSIEIAASALAMEYDVVPPTANLHTPDPECDLDYVPLT
DHAYRTPVSSI KSMVGHSLGAGSIEIAASALAMEYDVVPPTANLHTPDPECDLDYVPLR
DHAYRVPVSSI KSMIGHSLGAGSLEIAASVLAITHDVVPPTANLHEPDPECDLDYVPLR
QRAYDVPVSSI KSMIGHSLGAGSLELAACALAI EHGVIPTANYEEDPECDLDYVPLT
DHAYRVPVSSI KSMIGHSLGAGSLEVAATATAVEYGAIPPTANLHDPDPELDLDYVPLT
EHAYRVPVSSI KSMIGHSLGAGSLEVAATATAVEYGVIPPTANLHDPDPELDLDYVPLT
EHAYATPMSSI KSMVGHSLGAGSIEIAACVLA MAHQVVPPTANYTTTPDPECDLDYVPRE
*:: :: * . :::: :::: :::: ::::

KCLFDAU
KCLFPEU
KCLFACT
KCLFHIR
KCLFGRA
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KCLFTCM
KCLFCIN
KCLFVNZ
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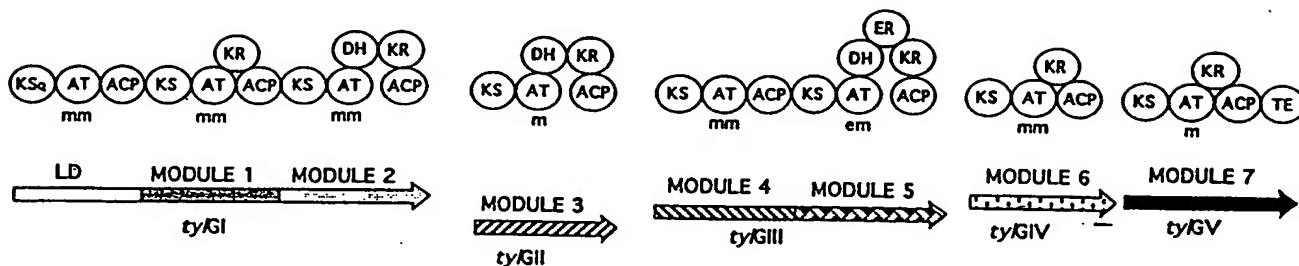
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VRPAALRTA-LGGARGHG GFNSALVVRAGQ-----
PRTAEVNTA-LVIARGHG GFNSAMVVRSAN-----
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AREQRVDIV-LTVGSGFGGFQ SAMVLHRPEEAA----
AREQRVDIV-LSVGSGFGGFQ SAMVLRRLGGANS---
ARERKLRSV-LTVGSGFGGFQ SAMVLRDAETAGAAA-
ARDQRVDSV-LTVGSGFGGFQ SAMVL TSAQ---RSTV
CREQLTDSV-LTVGSGFGGFQ SAMVLARPE---RKIA
ARACPVDTV-LTVGSGFGGFQ SAMVLCGPGSRGRSAA
AREQRVDIV-LSVGSGFGGFQ SAAVLARPKETR---
AREKVRHA-LTVGSGFGGFQ SAML LSRPER-----
AREKVRHA-LTVGSGFGGFQ SAML LSRLER-----
ARERTLRHV-LSVGSGFGGFQ SAVVLSGSEGGLR---
* . * . * * ::* ::

mole:-/ks2%

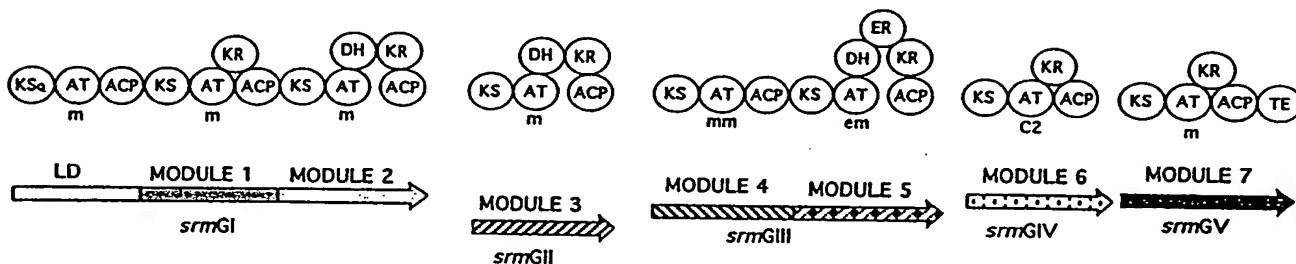
Fig 2D

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ORGANISATION OF THE TYLOSIN-PRODUCING POLYKETIDE SYNTHASE



ORGANISATION OF THE SPIRAMYCIN-PRODUCING POLYKETIDE SYNTHASE



ORGANISATION OF THE NIDDAMYCIN-PRODUCING POLYKETIDE SYNTHASE

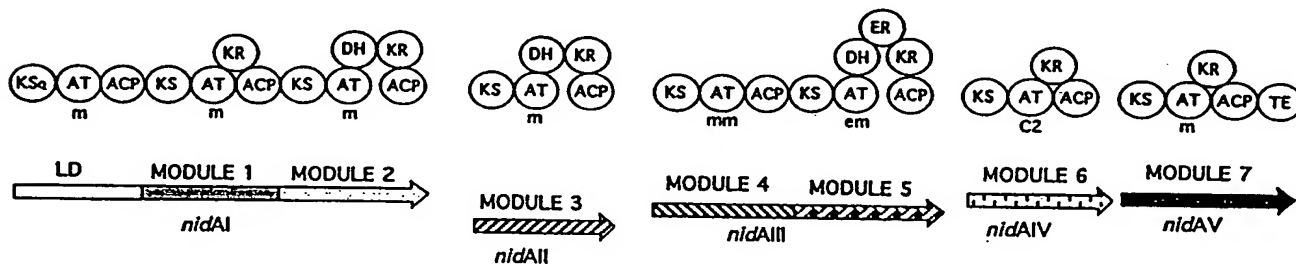


Fig 3

m: malonyl transferase
mm: methylmalonyl transferase
em: ethylmalonyl transferase
C2: unknown C2 unit transferase

Fig. 4A

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	1					50
niddamycin	-----	-----	MAGHGDATAQ	KAQDAEKSED	GSDAIAVIGM	
platenolide	-----	-----	-----MS	GELAISRSDD	RSDAVAVVGM	
monensin	-----	-----	-----MAAS	ASASPSGPSA	GPDPIAVVGM	
oleandomycin	-----	-----	-----	---MHVPGEE	NGHSIAIVGI	
tylosin	MSSALRRVQ	SNCGYGDLMT	SNTAAQNTGD	QEDVDGPDST	HGGEIAVVGM	
	51					100
niddam...	SCRFPGAPGT	AEFWQLLSSG	ADAVVTAADG	RRR.....GTIDA	
platenol.	ACRFPGAPGI	AEFWKLLTDG	RDAIGRDADG	RRR.....GMIEA	
monensin	ACRLPGAPDP	DAFWRLLESG	RSAVSTAPPE	RRRADSGLHG	P...GGYLDR	
oleandom	ACRLPGSATP	QEFWRLLADS	ADALDEPPAG	RFPTGSLSSP	PAPRGGFLDS	
tylosin	SCRLPGAAGV	EEFWELLRSR	RGMPTRQDDG	TWRAA.....LED	
	101					150
niddam...	PADFDAAFFG	MSPREAAATD	PQORLVLELG	WEALEDAGIV	PESLRGEAAS	
platenol.	PGDFDAAFFG	MSPREAAETD	PQORLMLELG	WEALEDAGIV	PGSLRGEAVG	
monensin	IDGFDADFFH	ISPRAVAMD	PQORLLELS	WEALEDAGIR	PPTLARSRTG	
oleandom	IDTFDADFFN	ISPRAEGLD	PQORLLELG	WEALEDAGIV	PRHLRGTRTS	
tylosin	HAGFDAGFFG	MNARQAAATD	PQHRLMLELG	WEALEDAGIV	PGDLTGTDG	
	151					200
niddam...	VFVGAMNDY	ATLLH.RAGA	PTDITYTATGL	QHSMIANRLS	YFLGLRGPSL	
platenol.	VFVGAMHDDY	ATLLH.RAGA	PVGPHATATGL	QRAMLNRLS	YVLGTRGPSL	
monensin	VFVGAFWDDY	TDVLNLRAPG	AVTRHTMTGV	HRSILANRIS	YAYHLAGPSL	
oleandom	VFMGAMWDDY	AHLAHARGE	ALTRHSLTGT	HRGMIANRLS	YALGLQGPSL	
tylosin	VFAGVASDDY	A.VLTRRSV	SAGGYTATGL	HRALANRLS	HFLGLRGPSL	
	201					250
niddam...	VVDTGQSSSL	VAVALAVESL	RGGTSGIALA	GGVNLVLAEE	GS.AAMERVG	
platenol.	AVDTAQSSSL	VAVALAVESL	RAGTSRVAVA	GGVNLVLADE	GT.AAMERLG	
monensin	TVDTAQSSSL	VAVHLACESI	RSGDSIAFA	GGVNLICSPR	TTELAARFG	
oleandom	TVDTGQSSSL	AAVHMACE	ARGESDLALV	GGVNLVLDPA	GT.TGVERFG	
tylosin	VVDSAQSASL	VAVQLACESL	RRGETSLAVA	GGVNLILTEE	ST.TVMERMG	
	251					300
niddam...	ALSPDGRCHT	FDARANGYVR	GEGGAIVVLK	PLADALADGD	RVYCVVRGVA	
platenol.	ALSPDGRCHT	FDARANGYVR	GEGGAIVVLK	PLADALADGD	PVYCVVRGVA	
monensin	GLSAAGRCHT	FDARADGFVR	GEGGLVVLK	PLAAARRDGD	TVYCVIRGSA	
oleandom	ALSPDGRCHT	FDSRANGYAR	GEGGVVVVLK	PTHRALADGD	TVYCEILGSA	
tylosin	ALSPDGRCHT	FDARANGYVR	GEGGAVVLK	PLDAALADGD	RVYCVIKGGA	
	301					350
niddam...	TGNDGGGPGL	TVPDRAGQEA	VLRAACDQAG	VRPADVRFVE	LHGTGTPAGD	
platenol.	VGNDGGGPGL	TAPDREGQEA	VLRAACAQAR	VDPAEVRFVE	LHGTGTPVGD	
monensin	VNSDGTDDGI	TLPSGQAQD	VVRLACRRAR	ITPDQVQYVE	LHGTGTPVGD	
oleandom	LNNDGATEGL	TVPSARAQAD	VLRAQAWERAR	VAPTDVQYVE	LHGTGTPAGD	
tylosin	VNNDGGGASL	TTPDREAQEA	VLRAQAYRRAG	VSTGAVRYVE	LHGTGTRAGD	

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	351		400
niddam...	PVEAEALGAV YGTGRP..AN EPLLVGSVKT NIGHLEGAAG IAGFVKAALC		
platenol.	PVEAHALGAV HGSGRP..AD DPLLVGSVKT NIGHLEGAAG IAGLVKAALC		
monensin	PIEAAALGAA LGQDAA..RA VPLAVGSAKT NVGHLEAAAG IVGLLKTALS		
oleandom	PVEAEGLGTA LGTARP..AE APLLVGSVKT NIGHLEGAAG IAGLLKTVLS		
tylosin	PVEAAALGAV LGAGADSGRS TPLAVGSVKT NVGHLEGAAG IVGLIKATLC		
	401		450
niddam...	LHERALPASL NFETPNPAIP LERLRLKVQT AHAALQPGTG GGPLLAVGSA		
platenol.	LRERTLPGSL NFATPSPAIP LDQLRLKVQT AAAELPLAPG GAPLLAGVSS		
monensin	IHHRRLAPSL NFETPNPAIP LADLGLTVQQ DLADWP..RP EQPLIAGVSS		
oleandom	IKNRHLPASL NFETSPNPRID LDALRLRVHT AYGPWP..SP DRPLVAGVSS		
tylosin	VRKGELVPSL NFSTPNPDIP LDDLRLRVQT ERQEW.NEED DRPRVAGVSS		
	451		500
niddam...	FGMGGTNCHV VLEETPGG..RQPAE.T	
platenol.	FGIGGTNCHV VLEHLPSR..PTPAV.S	
monensin	FGMGGTNCHV VVA....AAP DSVAVPEPVG VPERVEVPEP VVVSEPVVVP		
oleandom	FGMGGTNCHV VLSELRNAGG DGAGKGPYTG TEDRLGATEA EKRPDPATGN		
tylosin	FGMGGTNVHL VIAEAPAAAG SSGAGGSGAG SGAGISAVSG VV.....		
	501		550
niddam...	GQADACLFSA SPMLLLSARS EQALRAQAAR LREHL..EDS GADPLDIAYS		
platenol.	VAAS...LPD VPPLLLSARS EGALRAQAVR LGETV..ERV GADPRDVAYS		
monensin	TPWP.....VSAHS ASALRAQAGR LRTHLAAHRP TPDAARVGH	
oleandom	GPDPAQDTHR YPALILSARS DAALRAQAER LRHHL.EHSP GQRLRDTAYS		
tylosinPVVVSGRS RVVVREAAGR LAE..VVEAG GVGLADVAVT		
	551		600
niddam...	LATTRTRFEH RAAVPCGDPD RLSSALAALA AGQTPRGVRI GS..TDADGR		
platenol.	LASTRTLFEH RAVVPCGGRG ELVAALGGFA AGRVSGGVRS GR..A.VPGG		
monensin	LATTRAPLAH RAVLLGGDTA ELLGSLDALA EGAETASIVR GEAYT..EGR		
oleandom	LATTRQVFER HAVVTGHDRE DLLNGLRDLE NGLPAPQVLL GRTPTPEPGG		
tylosin	MAD.RSRFGY RAVVLARGEA ELAGRLRALA GGDPDAGVVT G...AVLDGG		
	601		650
niddam...	LALLFTGQGA QHPGMGQELY TTDPHFAAAL DEVCEELQRC GTQNLREVMF		
platenol.	VGVLFSGQGA QWVGMGRGLY AGGGVFAEVL DEVLSMVGEV DGRSLRDVMF		
monensin	TAFLFSGQGA QRLGMGRELY AVFPVFADAL DEAFALDVH LDRPLREIVL		
oleandom	LAFLFSGQGS QPFGMKRLH QVFPGFRDAL DEVCAELDTH LGRL.....		
tylosin	VVVGAAAPGA GAAGGAGAAG GAGGGGVVLV FPGQGTQWVG MGAGLLGSSE		
	651		700
niddam...	TPDQPD....	LLDRTEYTQP ALFALQTALY	
platenol.	GDVDVDAGAG ADAGAGAGAG VSGSGSVGG LLGRTEFAQP ALFALEVALF		
monensin	GETDSGGNVS GENVIGEGA.DHQA LLDQTAYTQP ALFAIETSLY		
oleandom	.GPEAGPPLR DVMFAERGT.AHSA LLSETHYTQA ALFALETALF		
tylosin	VFAASMRECA RALSVHVGWD LLEVVSAGG .LERVDVVQP VTWAVMVSLA		
	701		750
niddam...	RTLTARGETQA HVLGHGSVGE ITAAHIAGVL DLPDAARLIT ARAHVMGQLP		
platenol.	RALTEARGVEV SVVLGHGSVGE VAAATVAGVL SLGDAVRLVV ARGGLMGGLP		
monensin	RLAASFGLKP DYVLGHGSVGE IAAAHVAGVL SLPDASALVA TRGRMLQAVR		
oleandom	RLLVQWGLKP DHLAGHSVGE IAAHAAGIL DLSDAAELVA TRGALMRSIP		
tylosin	RYWQAMGVDV AAVVGHSSQGE IAAATVAGAL SLEDAAAVVA LRAGLIGRYL		

Fig 4B

↑

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	751		800
niddam...	HG.GAMLSVQ	AAEHDLDQLA	HTHG..VEIA AVNGPTHCVL SGPRTALEET
platenol.	VG.GGMWSVG	ASESVVRGVV	EGLGEWVSVA AVNGPRSVVL SGDVGVLSEV
monensin	AP.GAMAAWQ	ATADEAAEQL	AGHERHVTVA AVNGPDSVVV SGDRATVDEL
oleandom	GG.GVMLSQ	APESVAPLL	LGREAHVGLA AVNGPDAVVV SGERGHVAAI
tylosin	AGRGAMAAVP	LPAGEVEAGL	.AKWPGVEVA AVNGPASTVV SGDRRAVAGY
	801		850
niddam...	AQHLREQNVR	HTWLKVSHAF	HSALMDPMLG AFRDTLNTLN Y..QPPTIPL
platenol.	VASLMGDGVE	YRRLDVSHGF	HSVLMEPVLG EFRGVVESLE FGRVRPGVVV
monensin	TAAWRGRGRK	AHHLKVSHAF	HSPHMDPILD ELRAVAAGLT FHE..PVIPV
oleandom	EQILRDRGRK	SRYLRVSHAF	HSPLMEPVLE EFAEAVAGLT FRA..PTTPL
tylosin	VAVCQAEQVQ	ARLIPVDYAS	HSRHVEDLKG ELERVLSGI. .RPRSPRPV
	851		900
niddam...	ISNLTGQIA.DPNHL	CTPDYWIDHA RHTVRFADAV QTAHHQGT
platenol.	VSGVSGGVV.GSGEL	GDPGYWVRHA REAVRFADGV GVVRLGVGT
monensin	VSNVTGELVT	ATATGSGAGQ	ADPEYWARHA REPVRFLSGV RGLCERGVT
oleandom	VSNLTG....	..APVDDRTM	ATPAYWVRHV REAVRFGDGI RALGKLGTGS
tylosin	CSTVAGEQPG	EPVF.....	.DAGYWFRNL RNRVEFSAVV GGLLEEGRH
	901		950
niddam...	YLEIGPHPTL	TTLHHTL..	.DNP.....T TIPTLHRERP
platenol.	LVEVGPHGVL	TGMAGECLGA	GDDV.....V VVPAMRRGRA
monensin	FVELGPDAPL	SAMARCFPA	P.....ADRSRPRPA AIATCRRGRD
oleandom	FLEVGPDGVL	TAMARACVTA	APEPGHRGEQ GADADAHTAL LLPALRRGRD
tylosin	FIEVSAHPVL	V.....HAIEQ TAEAADRSVH ATGTLRRQDD
	951		
niddam...	EPETLTQAIA	AVGVRTDGID	WAVLCGASRP RRVELPTYAF
platenol.	EREVFEAALA	TVFTRDAGLD	ATALHTGSTG RRIDLPTTPF
monensin	EVATFLRSLA	QAYVRGADVD	FTRAYGATAT RRFPLPTYPF
oleandom	EARSLTEAVA	RLHLHGVPMD	WTSVLGGDVS .RVPLPTYAF
tylosin	SPHRLLTSTA	EAWAHGATLT	WDPAL..PPG HLTTLPTYPF

niddam: niddamycin; platenol: platenolide I (spiramycin); oleandom:
oleandomycin.

FIG. 4C

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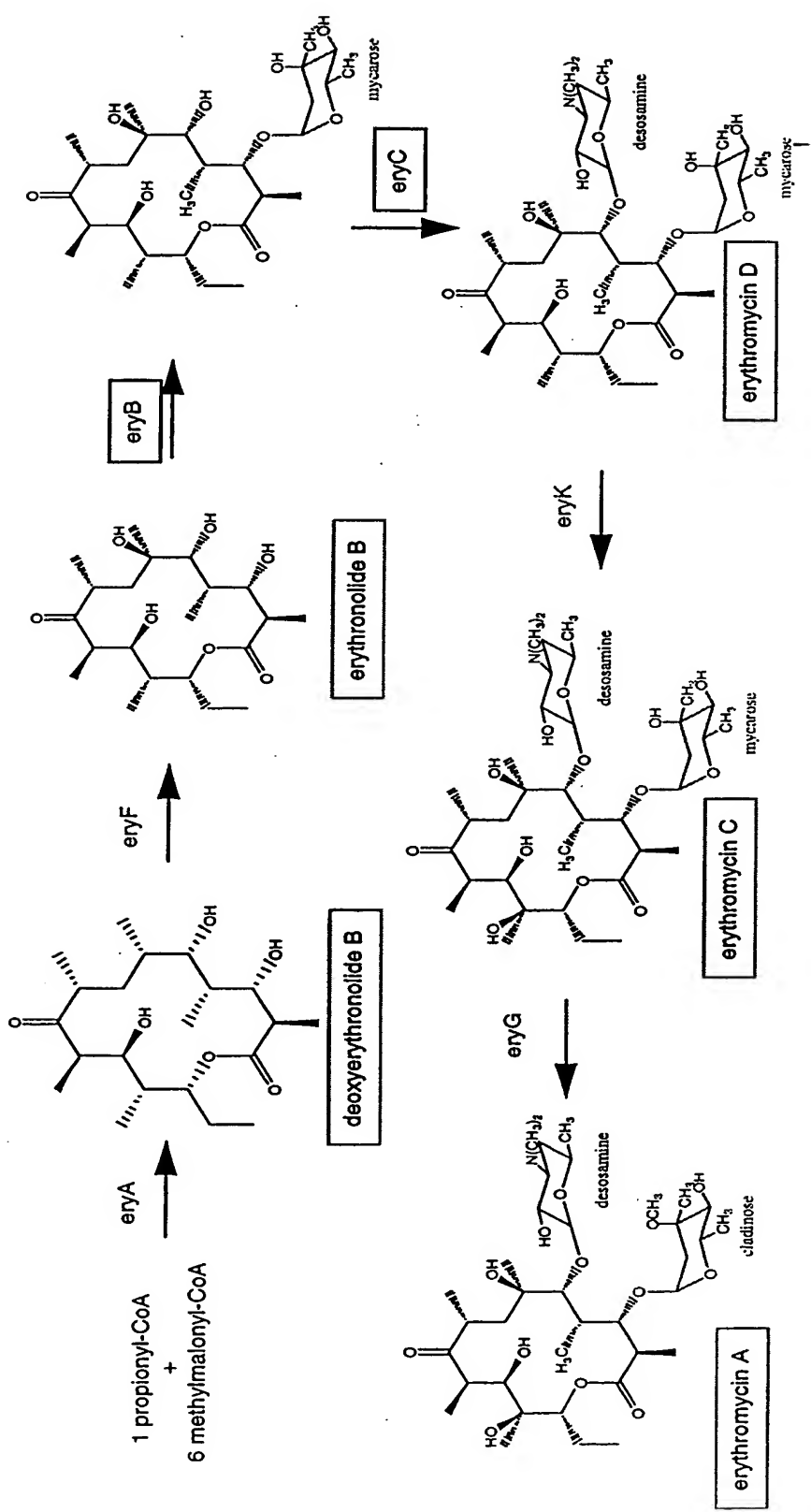


Fig. 5

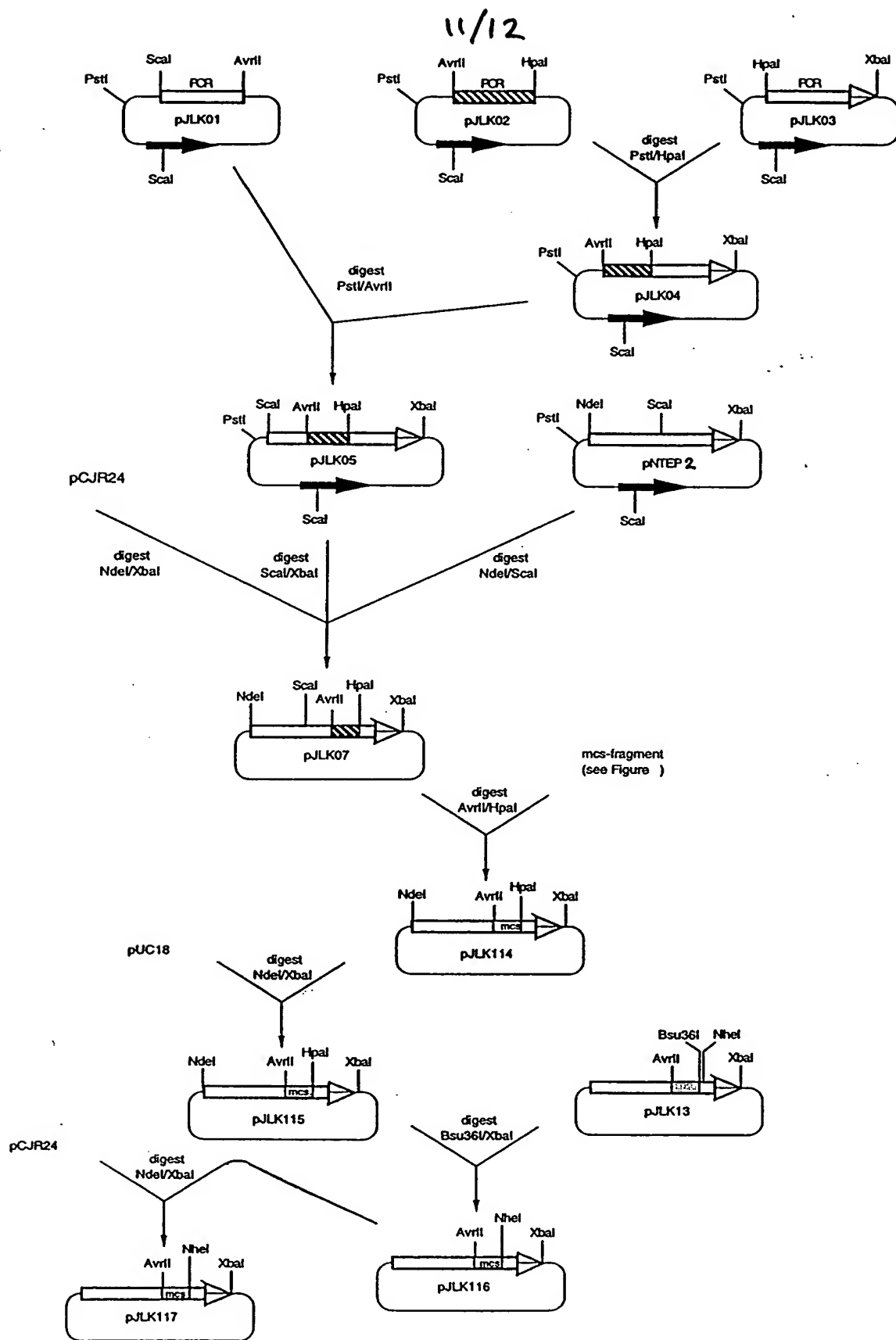


Fig 6

Figure 7

forward (Plf):

5'-CTA GGC CGG GCC GGA CTG GTA GAT CTG CCT ACG TAT CCT TTC CAG GGC AAG CGG TTC TGG CTG CAG CCG GAC CGC ACT AGT CCT CGT GAC GAG

GGA GAT GCA TCG AGC CTG AGG GAC CGG TT-3'

backward (Plb):

5'-AAC CGG TCC CTC AGG CTC GAT GCA TCT CCC TCG TCA CGA GGA CTA GTG CGG TCC GGC TGC AGC CAG AAC CGC TTG CCC TGG AAA GGA TAC GTA

GGC AGA TCT ACC AGT CCG GCC CGG C-3'

oligos annealed:

CTAGCCCGGCGGACTGGTAGATCTGCCTACGTATACCTTTCCAGGGCAAGCGGTTCTGGCTGCAGCCGGACCGCACTAGTCTCTGTGACGAGGGAGATCCATCGAGCCTGAGGGACCGGTT
CGGCGGCGGCTGACCATCTAGACGGATGCAATAGGATCCCGTTCCCAAGACCGACGTCGGCCTGGCGTGATCAGGAGCACTGCTCCCTCTACGTAGCTCGGACTCCCTGGCCAA

AvrII BglII SnaBI PstI SpeI NsiI Bsu36I HpaI
